

Remarks

Applicant thanks the Examiner for kindly withdrawing all of the previously pending rejections of record and implicitly acknowledging that Applicant's statements in the August 2, 2007 Amendment overcame the same.

There being no rejection outstanding against claims 27, 43, and 88, Applicant respectfully requests that the next action include an indication as to the allowability of the same.

Claims 30, 2, 3, 5-11, 13-19, 22, 25, 26, 31-42, 44-47, 56-65, 84-86, and 89-92 stand rejected under 35 U.S.C. § 103 over Schultz (U.S. Patent 6,256,522) in view of Empedocles et al. (U.S. Published Application 2002/0031783).

Schultz describes a sensor unit (4) that can be implanted under the skin (6), a light source 30 that can illuminate the sensor unit (4), and a detector (44) that can measure a property of the system (Schultz, col. 7, lines 11-16). The sensor unit (4) includes a capsule that includes a semipermeable membrane (8) that is permeable to analyte (12), analog-analyte molecules (14) that are covalently bonded to dye molecules (16), and receptor molecules (20) covalently bonded to dye molecules (22) (*Id.*, col. 9, lines 1-21). Schultz discloses that the liquid in the capsule preferably is the equivalent of plasma (*Id.*, col. 6, lines 28-29). The light source (30) causes light beam (32) to pass through the skin (6) to illuminate a dye molecule (e.g., 16, 22), which causes a responsive fluorescent light to emerge through the skin (6) in the form of a beam (42), which is received by the detector (44) (*Id.*, col. 9, lines 22-33).

Empedocles et al. describe a two dimensional spectral imaging system that detects and identifies signals from within a signal area (Empedocles et al., page 1, para. [0003]). More specifically Empedocles et al. describe a system for detecting and identifying spectral barcodes from a sensing area, which they frequently describe as being a two dimensional array. According to Empedocles et al., the method can be used to identify and track inventories of elements, and in high-throughput assay systems (*Id.*).

As a preliminary matter, Applicant wishes to note that he does not understand the logic set forth at page 3, second full paragraph, of the October 18, 2007 Office action regarding why it would be obvious to combine Empedocles et al. and Schultz. To the

extent the rejection of claim 30 is maintained, Applicant respectfully requests clarification thereof.

Claim 30 is directed to a system for detecting an analyte where the system includes a sensor adapted to detect the analyte, the sensor including a polymer matrix, fluorophores, and a membrane surrounding the polymer matrix, an excitation source to excite a fluorophore of the sensor, a first detector adapted to detect light of a first wavelength emitted by the sensor, a second detector adapted to detect light of a second wavelength emitted by the sensor, a third detector adapted to detect light of a third wavelength, and a processor for processing signals corresponding to light detected by the detectors and for determining a property of the analyte. “[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int’l Co. v. Teleflex Inc.*, 500 U.S. \_\_\_\_, 82 U.S.P.Q.2d 1385 (2007) quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). A claim “composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *Id.* (Emphasis added.) Rather, it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *Id.* “[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.*

To support the rejection of claim 30, the October 18<sup>th</sup> Office action implies that Schultz seeks to detect a number of analytes and in a faster and more efficient manner (see, October 18<sup>th</sup> Office action, page 3, lines 9-12). However, Schultz does not seek to detect a number of analytes and in a faster and more efficient manner. Rather, Schultz seeks to detect the amount of analyte present in a fluid (e.g., a bodily fluid) in real time using an implantable sensor (e.g., disposed *in vivo* in a human being). Moreover, it is not the detectors of Empedocles et al. that allow Empedocles et al. to conduct multiple analyses; rather, it is the spectral codes employed by Empedocles et al. that facilitate the achievement of their analyses. Therefore, the reasoning asserted in the October 18<sup>th</sup> Office action for finding claim 1 obvious over Schultz in view of Empedocles et al. is not

sound, and Applicant submits that the rejection cannot be maintained on the asserted basis.

The proposed rejection of claim 1 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. is further unwarranted for at least the following additional reasons. Schultz seeks to detect the amount of an analyte present in a fluid by studying the amount of analyte that enters his implantable sensor. Schultz focuses on *in vivo* uses of his sensor.

Empedocles et al. are not concerned with detecting the amount of analyte present in a fluid or *in vivo* applications. The focus of Empedocles et al. is on identifying the specific elements in a library utilizing a spectral code (see, e.g., Empedocles et al., para. [0071]). Empedocles et al. explain that their techniques “find advantageous application within highly multiplexed assays, inventory control in which a large number of small and/or fluid elements are intermingled, and the like” (*Id.*, para. [0063]). Empedocles et al. are further focused on identifying the optical and positional characteristics of moieties based on an optical spectral code. Although Empedocles et al. disclose that their spectral codes can be used in conjunctions with assays, the assays described by Empedocles et al. are highly multiplexed and involve high throughput assays in which a number of assays are performed and a number of assay signals are generated to determine the assay results (see, e.g., *Id.*, para [0037]). The sensor of Schultz, in contrast, is not intended for use with high throughput assays. To the contrary, it is designed to detect the presence and amount of an analyte in a fluid, e.g., a bodily fluid, using a sensor (see, e.g., Schultz, col. 8, lines 46-53, col. 9, lines 1-3). Empedocles et al. do not teach or suggest utilizing their system, or at least three detectors, in conjunction with a sensor that determines the amount of an analyte present in a fluid. Empedocles et al. also do not teach or suggest utilizing their system, or at least three detectors, in conjunction with a sensor that includes fluorophores and a membrane that surrounds a polymeric matrix. Therefore, the skilled artisan familiar with Schultz would have no reason to look to Empedocles et al. and further would find Empedocles et al. to have no bearing on Schultz.

Moreover, to arrive at the system of claim 30 from the proposed combination of Schultz and Empedocles et al., the skilled artisan would have not make a series of selections. In particular, the skilled artisan would have to select a sensor configuration

from Schultz that includes a polymer matrix when Schultz describes a gel as being only one of many possible components of his sensor construction. The skilled artisan would then have to decide to surround the polymer matrix with a membrane, when Schultz indicates that it is only necessary to have a membrane present. At no point does Schultz expressly teach surrounding a polymer matrix with a membrane. The skilled artisan would then have to decide to look to Empedocles et al. The skilled artisan is not an automaton (see, *KSR Int'l Co. v. Teleflex Inc.*, 500 U.S. \_\_\_\_ (2007)). The purpose and system of Empedocles et al. is in no way related to the purpose and sensor of Schultz. Therefore the skilled artisan would have no reason to look to Empedocles et al. If for some reason the skilled artisan did decide to look to Empedocles et al., the skilled artisan would then have to find some reason in Empedocles et al. for including at least three detectors in the system of Schultz. Nothing in Empedocles et al. teaches or suggests utilizing their system, or any component thereof, in combination with a sensor such as that disclosed in Schultz --let alone a sensor that includes a polymer matrix and a membrane surrounding the polymer matrix. Moreover, nothing in Empedocles et al. directs the skilled artisan to select three detectors for use in combination with the sensor of Schultz. Therefore, Empedocles et al. provides the skilled artisan with no reason to modify Schultz so as to achieve the system of claim 30. Accordingly, Applicant submits that the rejection of claim 30 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. has been overcome and respectfully requests that it be withdrawn.

Applicant now addresses certain statements in the October 18<sup>th</sup> Office action. The item of Empedocles et al. identified in the October 18<sup>th</sup> Office action as a membrane is actually a seven micron layer of parylene disposed on a glass surface that has been ablated, which ablation forms a number of seven micron deep wells. The layer of parylene of Empedocles et al. does not surround a polymer matrix. Empedocles et al. thus do not teach a sensor that includes a membrane surrounding a polymer matrix. Any assertion to the contrary in the October 18<sup>th</sup> Office action is incorrect.

Claims 2, 3, 5-11, 13-19, 22, 25, 26, 31-42, 44-47, 84-86, and 89-90 are distinguishable under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. for at least the reasons set forth above in distinguishing claim 30. In addition, in an obviousness determination, the Patent Office bears the burden of explicitly setting forth

an analysis of the interrelated teachings of multiple patents, the effects of demands known to the design community or present in the marketplace, and the background knowledge possessed by a person having ordinary skill in the art that led to the determination of the apparent reason to combine the known elements in the fashion claimed. See, e.g., *KSR Int'l Co. v. Teleflex Inc.*, citing *In re Kahn*. It is implicit that such an analysis must be set forth in a manner that is understandable to a reasonable patent practitioner. Here, no such analysis has been provided for dependent claims 2, 3, 5-11, 13-19, 22, 25, 26, 31-42, 44-47, 84-86, and 89-90. Instead, particularly with respect to the dependent claims, the October 18<sup>th</sup> Office action merely identifies where in the cited reference an element of the claim can be found. Such an indication does not constitute an explicit analysis demonstrating what led to the determination that it would be obvious to combine Schultz and Empedocles in the manner set forth in Applicant's claims. Accordingly, Applicant submits that a *prima facie* case of obviousness has not been made with respect to any of dependent claims 2, 3, 5-11, 13-19, 22, 25, 26, 31-42, 44-47, 84-86, and 89-90. As such, the burden has not shifted to Applicant to rebut the same.

The rejection of claims 13, 14, 26, 41, 42, and 44-47 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. is further unwarranted for at least the following additional reasons. Claim 13 depends from claim 30 and further specifies that the fluorophores are mobile within the polymer matrix. The sensor unit (4) of Schultz does not include fluorophores that are mobile within a polymer matrix. Schultz explains that the liquid in the capsule of his sensor unit (4) is the equivalent of plasma (see Schultz, col. 6, lines 28-29). Schultz discloses that one embodiment of his sensor unit (4) includes a gel in the chamber of the sensor. In the embodiment that includes a gel, the receptor material is immobilized to the gel such that the receptor material is covalently bonded to strands of polymers, which are cross-linked to each other to form a gel (see, e.g., *Id.*, col. 6, lines 2-8). Schultz discloses that in order to cause fluorescence, and thereby allow detection, the analog-analyte should be fluorescently labeled by covalent coupling with an appropriate dye. Thus, Schultz discloses that the analog-analyte can include a fluorescent label. Schultz does not, however, teach or suggest that the analyte-analog is mobile within the cross-linked polymer gel when the gel is present. Schultz does not

teach or suggest that there are any fluorophores that are mobile within his gel. Schultz thus fails to teach a required element of claim 13.

Empedocles et al. do not cure the deficiencies of Schultz. Empedocles et al. do not teach or suggest anything about the construction of a sensor that includes a polymer matrix, fluorophores, and a membrane. Empedocles et al. further fail to teach or suggest fluorophores that are mobile within a polymer matrix. Nothing in the record establishes anything to the contrary. The only polymeric matrix identified in the October 18<sup>th</sup> Office action is the polymeric matrix mentioned at paragraph [0081] of Empedocles et al. (see, October 18<sup>th</sup> Office action, page 3, first full paragraph). Empedocles et al. disclose, “[Labeled] bodies may comprise a composition of matter including a polymeric matrix and a plurality of semiconductor nanocrystals, which can be used to encode discrete and different absorption and emission spectra” (Empedocles et al., page 8, para. [0081]). Nothing in this passage teaches or suggests that there are fluorophores in the polymeric matrix or that those fluorophore, even if present, are mobile within the polymeric matrix. The proposed combination of Schultz and Empedocles et al. thus fails to teach a required element of claim 13, i.e., fluorophores that are mobile within a polymeric matrix. As such, a *prima facie* case of obviousness of claim 13 has not been made. Accordingly, the rejection of claim 13 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of fluorophores that are mobile within a polymeric matrix.

Claim 14 depends from claim 30 and further specifies that the processor is adapted to store a value corresponding to a property of the detected analyte as a function of time. Neither Schultz nor Empedocles et al. teach or suggest a processor that is adapted to store a value corresponding to a property of the detected analyte as a function of time. Nothing in the record establishes anything to the contrary. Schultz and Empedocles et al. thus fail to teach a required element of the system of claim 14. Accordingly, a *prima facie* case of obviousness of claim 14 has not been made, and the burden has not shifted to Applicant to rebut the same. Thus, the rejection of claim 14 under 35 U.S.C. § 103 over the Schultz in view of Empedocles et al. cannot stand, and

Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a processor that is adapted to store a value corresponding to a property of the detected analyte as a function of time.

Claim 26 depends from claim 30 and further specifies that the system further includes a means for pulsing the light emitted by the excitation source. It is undisputed that Schultz does not teach a means for pulsing the light emitted by the excitation source.

Empedocles et al. do not cure the deficiencies of Schultz. The system of Empedocles et al. is nothing like that of Schultz. Empedocles et al. do not teach or suggest utilizing a means for pulsing the light emitted by the excitation source in combination with a sensor that includes a polymer matrix and a membrane surrounding the polymer matrix. Therefore the skilled artisan would have no reason to do so. Thus, for at least this additional reason, the rejection of claim 26 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. is unwarranted, and Applicant respectfully requests that it be withdrawn.

Claim 41 depends from claim 30 and further specifies that the third detector is adapted to detect light emitted by skin when the skin is excited by the excitation source. Neither Schultz nor Empedocles et al. teach or suggest a third detector adapted to detect light emitted by skin when the skin is excited by the excitation source. Nothing in the record establishes anything to the contrary. Schultz and Empedocles et al. thus fail to teach a required element of the system of claim 41. Accordingly, a *prima facie* case of obviousness of claim 41 has not been made, and the burden has not shifted to Applicant to rebut the same. Thus, for at least this additional reason, the rejection of claim 41 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. is unwarranted, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a third detector adapted to detect light emitted by skin when the skin is excited by the excitation source.

Claim 42 depends from claim 30 and further specifies that the processor is programmed with code to correct for the light emitted and scattered by the skin. Neither Schultz nor Empedocles et al. teach or suggest correcting for light emitted and scattered by skin. In addition, neither Schultz nor Empedocles et al. teach or suggest a processor programmed with code to correct for the light emitted and scattered by the skin. Nothing in the record establishes anything to the contrary. Schultz and Empedocles et al. thus fail to teach a required element of the system of claim 42. Accordingly, a *prima facie* case of obviousness of claim 42 has not been made, and the burden has not shifted to Applicant to rebut the same. Therefore, the rejection of claim 42 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand and must be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of processor is programmed with code to correct for the light emitted and scattered by the skin.

There being no further rejection of record pertaining to claim 42, Applicant submits that claim 42 is allowable and respectfully requests that the next action include an indication as to the same.

Claim 44 depends from claim 43 and further specifies that the processor further includes code to calculate a ratio of the corrected intensity at the first wavelength to the corrected intensity at the second wavelength. It is undisputed that neither Schultz nor Empedocles et al. nor the combination thereof teach or suggest the system of claim 43 (i.e., claim 43 is not rejected over Schultz in view of Empedocles et al., therefore any claim depending from claim 43 is also distinguishable over Schultz in view of Empedocles et al.). Accordingly, it is axiomatic that neither Schultz nor Empedocles et al. nor the combination thereof teach or suggest the system of claim 44. Moreover, nothing in either Schultz or Empedocles et al. teaches or suggests the processor that includes code to calculate a ratio of the corrected intensity at a first wavelength to the corrected intensity at a second wavelength. Nothing in the record establishes anything to the contrary. To support the rejection, the October 18<sup>th</sup> Office action includes assertions as to the capabilities of the sensor of Schultz. Applicant does not understand the relevance of the assertions in the October 18<sup>th</sup> Office action as to the capabilities of the



sensor. Speculation as to what a sensor might do is not a proper basis for an obviousness rejection. To establish obviousness, the proposed combination of references must teach or suggest each and every limitation in the claim at issue. Here the proposed combination of Schultz and Empedocles et al. fails to teach or suggest each and every element of the system of claim 44. Accordingly, for at least this additional reason, the rejection of claim 44 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand and must be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a processor that includes code to calculate a ratio of the corrected intensity at the first wavelength to the corrected intensity at the second wavelength. To the extent the basis asserted in the October 18<sup>th</sup> Office action in support of the rejection is maintained, Applicant respectfully requests clarification thereof.

Claims 45 and 46 are distinguishable under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. for at least the same reasons claim 43 is distinguishable.

Claim 47 is directed to the system of claim 30 and further specifies that the processor is programmed with code to receive data corresponding to a first  $I(\lambda_1)$ , a second  $I(\lambda_2)$ , and a third  $I(\lambda_3)$  intensity measured at a first  $\lambda_1$ , a second  $\lambda_2$ , and a third  $\lambda_3$  wavelength, respectively, correct the intensity at the first wavelength  $I(\lambda_1)$  based on the intensity at the third wavelength  $I(\lambda_3)$  and a first set of three predetermined correction functions  $D(\lambda_1)$ ,  $A(\lambda_1)$ ,  $B(\lambda_1)$ , and correct the intensity at the second wavelength  $I(\lambda_2)$  based on the intensity at the third wavelength  $I(\lambda_3)$  and a second set of three predetermined correction functions  $D(\lambda_2)$ ,  $A(\lambda_2)$ ,  $B(\lambda_2)$ . Neither Schultz nor Empedocles et al. teach or suggest a processor that is programmed with code to correct the intensity at a first wavelength based on the intensity at the third wavelength and a first set of three predetermined correction functions, and to correct the intensity at the second wavelength based on the intensity at the third wavelength and a second set of three predetermined correction functions. The proposed combination thus fails to teach a required element of the system of claim 47. Accordingly, for at least this additional reason the rejection of claim 47 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand and must be withdrawn. Should this rejection be maintained, Applicant respectfully

requests that the next action identify, by reference to page or column and line number, the location in the cited references of the requisite teaching or suggestion.

Claim 56 is directed to a device that includes a detector-emitter array for detecting an analyte, the detector-emitter array including an excitation source adapted to excite a fluorophore of a sensor that includes fluorophores, and a chip that includes a first detector adapted to detect fluorescence light of a first wavelength emitted by the sensor, a second detector adapted to detect fluorescence light of a second wavelength emitted by the sensor, and a third detector adapted to detect light of a third wavelength, the excitation source being coupled to the chip. Neither Schultz nor Empedocles et al. teach or suggest a detector emitter array that includes a chip that includes three detectors and an excitation source coupled to the chip. Moreover, nothing in Schultz or Empedocles et al. teaches or suggests a chip that includes a first detector adapted to detect fluorescence light of a first wavelength emitted by a sensor or a second detector adapted to detect fluorescence light of a second wavelength emitted by the sensor. Nothing in the record establishes anything to the contrary. Accordingly, a *prima facie* case of the obviousness of claim 56 has not been made. Therefore, the rejection of claim 56 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand and must be withdrawn.

Claims 57-65 are distinguishable under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. for at least the reasons set forth above in distinguishing claim 30.

Claims 58 and 59 are further distinguishable under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. for at least the following additional reasons. Claim 58 depends from claim 56 and specifies that the excitation source is adapted to transcutaneously excite a fluorophore of the sensor. Neither Schultz nor Empedocles teach or suggest coupling an excitation source that is adapted to transcutaneously excite a fluorophore of a sensor to a chip that includes at least three detectors. Nothing in the record establishes anything to the contrary. Instead, the October 18<sup>th</sup> Office action asserts that Schultz discloses that the sensor is capable of exciting light transcutaneously and cites column 7, lines 10-20 in support of the same (see, October 18<sup>th</sup> Office action, page 3, para. 7). This is not true. Schultz does not disclose that his sensor is capable of exciting light transcutaneously. Rather, Schultz discloses that the sensor unit (4) can be illuminated remotely by a light source above the skin (see, Schultz, col. 7, lines 38-39).

(Emphasis added.) The October 18<sup>th</sup> Office action does not provide a reason the skilled artisan would utilize an excitation source that is adapted to transcutaneously excite a fluorophore of a sensor in combination with a chip that includes three detectors. Since this reasoning has not been provided, a *prima facie* case of obviousness has not been made and the burden has not shifted to Applicant to rebut the same.

Even so, Applicant further notes that Empedocles et al. repeatedly emphasize that their image is obtained from a two-dimensional field and that the labeled elements must be on or near the surface for their system to work (“Imaging is facilitated by maintaining the labeled elements on or near a surface” (Empedocles et al., para. [0066]); “The detector images elements (12) from within a two-dimensional sensing field” (*Id.*, at [0067])). Therefore, the skilled artisan would have no reason to couple a detector of Empedocles et al. to an excitation source that is adapted to transcutaneously excite a fluorophore of a sensor and further would have no reasonable expectation of success. For at least this additional reason, the rejection of claim 58 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand, and Applicant respectfully requests that it be withdrawn.

Claim 59 depends from claim 56 and specifies that the detector is adapted to transcutaneously detect light emitted by the sensor. Neither Schultz nor Empedocles et al. teach or suggest a chip that includes three detectors in which at least one detector is adapted to transcutaneously detect light emitted by a sensor. Nothing in the record establishes anything to the contrary. Instead, the October 18<sup>th</sup> Office action asserts that Schultz discloses that the sensor is capable of exciting and detecting ultraviolet light and cites column 8, lines 28-37 of Schultz in support of the same (see, October 18<sup>th</sup> Office action, page 3, para. 7). This is not an accurate characterization of Schultz. Schultz does not disclose that his sensor is capable of exciting and detecting ultraviolet light. Moreover, the October 18<sup>th</sup> Office action does not provide a reason the skilled artisan would include a detector that is adapted to transcutaneously detect light emitted by a sensor in a chip that includes three detectors. Since this reasoning has not been provided, a *prima facie* case of obviousness of claim 59 has not been made and the burden has not shifted to Applicant to rebut the same.

Even in the absence of the required reasoning, Applicant notes that Empedocles et al. do not teach or suggest using their detector transcutaneously. Empedocles et al. also do not teach or suggest that their detector can function transcutaneously. To the contrary, it is very important that the labeled elements of Empedocles et al. be located near a surface. In addition, Empedocles et al. repeatedly emphasize that their image is obtained from a two-dimensional field and that the labeled elements must be on or near the surface for their system to work (“Imaging is facilitated by maintaining the labeled elements on or near a surface” (Empedocles et al., para. [0066]); “The detector images elements (12) from within a two-dimensional sensing field” (*Id.*, at [0067])). Therefore, the skilled artisan would have no reason to create a chip that includes a detector that is adapted to transcutaneously detect fluorescence light of a first wavelength and further would have no reasonable expectation of creating a useful device. Therefore, the skilled artisan would refrain from using the detector of Empedocles et al. in combination with the excitation source of Schulz and would have no clue as to how to modify the detector of Empedocles et al. such that it would work transcutaneously. For at least these additional reasons, the rejection of claim 59 under 35 U.S.C. § 103 over the Schultz in view of Empedocles et al. is unwarranted, and Applicant respectfully requests that it be withdrawn.

Claim 91 is directed to a system for detecting an analyte, the system including a sensor adapted to detect the analyte, the sensor comprising a polymer matrix, fluorophores, and a membrane, an excitation source to excite a fluorophore of the sensor, a first detector adapted to detect light of a first wavelength emitted by the sensor, a second detector adapted to detect light of a second wavelength emitted by the sensor, a third detector adapted to detect light of a third wavelength, a processor for processing signals corresponding to light detected by the detectors and for determining a property of the analyte, and a pump adapted to receive an instruction from the processor and to deliver an amount of a medicament, in response to the instruction. Neither Schultz nor Empedocles et al. teach or suggest a pump adapted to receive an instruction from the processor and to deliver an amount of a medicament, in response to the instruction --let alone a system for detecting an analyte that includes such a pump. Nothing in the record establishes anything to the contrary. Therefore a *prima facie* case of obviousness of

claim 91 has not been made, and the burden has not shifted to Applicant to rebut the same. Accordingly, the rejection of claim 91 under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. cannot stand, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a pump adapted to receive an instruction from the processor and to deliver an amount of a medicament, in response to the instruction.

There being no further rejection of record pertaining to claim 91, Applicant submits that claim 91 is allowable and respectfully requests that the next action include an indication as to the same.

Claim 92 is directed to a system for detecting an analyte, the system including a sensor adapted to detect the analyte, the sensor comprising a polymer matrix, fluorophores, and a membrane, the fluorophores being mobile within the polymer matrix, an excitation source to excite a fluorophore of the sensor, a first detector adapted to detect light of a first wavelength emitted by the sensor, a second detector adapted to detect light of a second wavelength emitted by the sensor, a third detector adapted to detect light of a third wavelength, and a processor for processing signals corresponding to light detected by the detectors and for determining a property of the analyte. The sensor unit (4) of Schultz does not include fluorophores that are mobile within a polymer matrix. Schultz explains that the liquid in the capsule of his sensor unit (4) is the equivalent of plasma (see Schultz, col. 6, lines 28-29). Schultz discloses that one embodiment of his sensor unit (4) includes a gel in the chamber of the sensor. In the embodiment that includes a gel, the receptor material is immobilized to the gel such that the receptor material is covalently bonded to strands of polymers, which are cross-linked to each other to form a gel (see, e.g., *Id.*, col. 6, lines 2-8). Schultz does not teach or suggest that there are any fluorophores that are mobile within his gel. Schultz discloses that in order to cause fluorescence, and thereby allow detection, the analog-analyte should be fluorescently labeled by covalent coupling with an appropriate dye. Thus, Schultz discloses that the analog-analyte can include a fluorescent label. Schultz does not, however, teach or

suggest that the analyte-analog is mobile within the cross-linked polymer gel when the gel is present. Schultz thus fails to teach a required element of claim 92.

Empedocles et al. do not cure the deficiencies of Schultz. Empedocles et al. do not teach or suggest anything about the construction of a sensor that includes a polymer matrix, fluorophores, and a membrane. Empedocles et al. further fail to teach or suggest fluorophores that are mobile within a polymer matrix. Nothing in the record establishes anything to the contrary. The only polymeric matrix identified in the October 18<sup>th</sup> Office action is the polymeric matrix mentioned at paragraph [0081] of Empedocles et al. (see, October 18<sup>th</sup> Office action, page 3, first full paragraph). Empedocles et al. disclose, “[Labeled] bodies may comprise a composition of matter including a polymeric matrix and a plurality of semiconductor nanocrystals, which can be used to encode discrete and different absorption and emission spectra” (Empedocles et al., page 8, para. [0081]). Nothing in this passage teaches or suggests that there are fluorophores in the polymeric matrix or that those fluorophore, even if present, are mobile within the polymeric matrix. The proposed combination of Schultz and Empedocles et al. thus fails to teach a required element of claim 92, i.e., fluorophores that are mobile within a polymeric matrix. As such a *prima facie* case of obviousness of claim 92 has not been made, and the rejection of claim 92 under 35 U.S.C. § 103 cannot stand. Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of fluorophores that are mobile within a polymeric matrix.

There being no further rejection of record pertaining to claim 92, Applicant submits that claim 92 is allowable and respectfully requests that the next action include an indication as to the same.

Claims 12, 20, 21, and 23 stand rejected under 35 U.S.C. § 103 over Empedocles et al. (U.S. Published Application 2002/0031783) in view of Martin et al. (U.S. Published Application 2002/0016535).

Empedocles et al. describe a two dimensional spectral imaging system that detects and identifies signals from within a signal area (Empedocles et al., page 1, para. [0003]). More specifically Empedocles et al. describe a system for detecting and identifying

spectral barcodes from a sensing area. According to Empedocles et al., the method can be used to identify and track inventories of elements, and in high-throughput assay systems (*Id.*).

Martin et al. disclose sensors such as glucose sensor that can be implanted in the human body (see, e.g., Martin et al., page 1, para. [0002]).

Claim 12 depends from claim 30 and further requires a pump adapted to receive an instruction from the processor and to deliver an amount of a medicament, in response to the instruction. Empedocles et al. do not teach or suggest a sensor that includes a polymer matrix surrounded by a membrane, as required by claim 12. Empedocles et al. also do not teach or suggest a pump adapted to receive an instruction from the processor and to deliver an amount of a medicament, in response to the instruction --let alone a system for detecting an analyte that includes such a pump. Nothing in the record establishes anything to the contrary.

Martin et al. do not cure the deficiencies of Empedocles et al. Martin et al. do not teach or suggest a polymer matrix surrounded by a membrane. Nothing in the record establishes anything to the contrary. Thus, a *prima facie* case of obviousness of claim 12 has not been established, and the burden has not shifted to Applicant to rebut the same. Moreover, since the proposed combination fails to teach or suggest an element of claim 12, the rejection of claim 12 under 35 U.S.C. § 103 over Empedocles et al. in view Martin et al. cannot stand, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a polymer matrix surrounded by a membrane.

Claims 20, 21, and 23 depend either directly or indirectly from claim 30 and thus are distinguishable under 35 U.S.C. § 103 over Schultz in view of Empedocles et al. for at least the reasons set forth above in distinguishing claim 12.

There being no further rejection of record pertaining to claims 12, 20, 21 and 23, Applicant submits that claims 12, 20, 21 and 23 are allowable and respectfully requests that the next action include an indication as to the same.

Claims 30, 2-4, 9-11, 13-19, 22, 24, 28, 29, 31, 32, 38-41, 45, 45, 56-65, and 89 stand rejected under 35 U.S.C. § 103 over Schultz (U.S. Patent 6,256,522) in view of Zenhausern (U.S. Published Application 2002/0094531).

The disclosure of Schultz set forth above is incorporated herein.

Zenhausern, which published on July 18, 2002, is directed to an apparatus and method for monitoring, analyzing and discriminating molecular species within a medium (Zenhausen, Abstract). Zenhausen discloses a method and device for detecting “and/or monitoring a biomolecule in a medium ... by using an assembly of at least one probing element for monitoring, preferably odorous, biomolecules or at least one secondary product of the biomolecule in gaseous and/or liquid form” (*Id.*, para. [0026]).

Zenhausern discloses that his invention provides a method and apparatus for a direct fast detecting and monitoring of unlabelled biomolecule cycling or amplification reactions (*Id.*, para. [0028]). Zenhausen further discloses that his method also includes the use of direct detection and monitoring of bimolecular reactions (e.g., polymerase chain reaction detection) in real-time without radioactive or fluorescent labeling (*Id.*, para. [0036]).

Zenhausern discloses that his method monitors information in a medium having at least one biomolecule and that the medium is preferably screened or analyzed in the gas phase (*Id.*, para. [0045]).

Claim 30 is directed to a system for detecting an analyte where the system includes a sensor adapted to detect the analyte, the sensor including a polymer matrix, fluorophores, and a membrane surrounding the polymer matrix, an excitation source to excite a fluorophore of the sensor, a first detector adapted to detect light of a first wavelength emitted by the sensor, a second detector adapted to detect light of a second wavelength emitted by the sensor, a third detector adapted to detect light of a third wavelength, and a processor for processing signals corresponding to light detected by the detectors and for determining a property of the analyte. “[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int’l Co. v. Teleflex Inc.*, 500 U.S. \_\_\_\_, 82 U.S.P.Q.2d 1385 (2007) quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). A claim “composed of several elements is not proved obvious merely by demonstrating that each of its elements was,



independently, known in the prior art.” *Id.* (Emphasis added.) Rather, it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *Id.* “[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.*

It is undisputed that Schultz fails to teach or suggest a system for detecting analyte that includes three detectors.

Zenhausern does not cure the deficiencies of Schultz. A person of ordinary skill is not an automaton. See, e.g., *Id.* The system of Zenhausern is nothing like the sensor of Schultz. The system of Zenhausern seeks to detect volatile components, e.g., gases evolved during PCR reactions (see, e.g., Zenhausern, paras [0080] and [0082]). The sensor of Schultz, in contrast, seeks to determine the amount of analyte present in a fluid (e.g., a bodily fluid) through a competitive binding reaction. The sensor of Schultz does not seek to monitor amplification processes. In addition, the sensor of Schultz is implantable. Zenhausern does not teach or suggest that his device is implantable nor is it inherently implantable. Moreover, nothing in Zenhausern teaches or suggests utilizing three detectors in combination with a sensor that includes a fluorophores, a polymer matrix and a sensor surrounding the polymer matrix. Therefore, skilled artisan familiar with the sensor of Schultz would have no reason to look to Zenhausern and further would find Zenhausern to have no bearing on the sensor of Schultz. It is only through hindsight that one would even attempt to cobble Schultz and Zenhausern together in an attempt to arrive at the system of claim 30. Hindsight is improper analysis on which to base an assertion of obviousness. Moreover, nothing in Zenhausern teaches or suggests that the detectors disclosed therein are capable of detecting fluorescence light. Therefore, the skilled artisan would have no reason to utilize the detectors of Zenhausern in combination with the sensor of Schultz.

The October 18<sup>th</sup> Office action asserts that “it would have been obvious to one of ordinary skill in the art ... to have used the multivariate detector of Zenhausern in the invention of Schultz, in order to extract useful information” and cites paragraph [0025] of Zenhausern in support thereof. Paragraph [0025] of Zenhausern discloses that the useful information extracted from the detector is used to control the measured process and/or

reaction, e.g., the polymerase chain reaction (see, Zenhusern, para. [0025]). Schultz does not seek to control the competitive binding reaction that occurs in his sensor. Therefore the motivation asserted in the October 18<sup>th</sup> Office action would not have motivated the skilled artisan to modify the system of Schultz. Applicant submits, therefore, that the rejection of claim 30 under 35 U.S.C. § 103 over Schultz in view of Zenhusern is unwarranted and respectfully requests that it be withdrawn.

Claims 2-4, 9-11, 13-19, 22, 24, 28, 29, 31, 32, 38-41, 45, 46, and 89 are under 35 U.S.C. § 103 over Schultz in view of Zenhusern for at least the reasons set forth above in distinguishing claim 30.

The rejection of claims 13, 14, and 41 under 35 U.S.C. § 103 over Schultz in view of Zenhusern is further unwarranted for at least the following additional reasons. Claim 13 depends from claim 30 and further specifies that the fluorophores are mobile within the polymer matrix. Notwithstanding the assertions to the contrary in the October 18<sup>th</sup> Office action, the sensor unit (4) of Schultz does not include fluorophores that are mobile within a polymer matrix. Schultz explains that the liquid in the capsule of his sensor unit (4) is the equivalent of plasma (see Schultz, col. 6, lines 28-29). Schultz discloses that one embodiment of his sensor unit (4) includes a gel in the chamber of the sensor. In the embodiment that includes a gel, the receptor material is immobilized to the gel such that the receptor material is covalently bonded to strands of polymers, which are cross-linked to each other to form a gel (see, e.g., *Id.*, col. 6, lines 2-8). Schultz discloses that in order to cause fluorescence, and thereby allow detection, the analog-analyte should be fluorescently labeled by covalent coupling with an appropriate dye. Thus, Schultz discloses that the analog-analyte can include a fluorescent label. Schultz does not, however, teach or suggest that the analyte-analog is mobile within the cross-linked polymer gel when the gel is present. Schultz does not teach or suggest that there are any fluorophores that are mobile within his gel. Schultz thus fails to teach a required element of claim 13.

Zenhusern does not cure the deficiencies of Schultz. Zenhusern does not teach or suggest a sensor that includes a polymer matrix and a membrane surrounding a polymer matrix. Zenhusern further fails to teach or suggest fluorophores that are mobile within a polymer matrix. Nothing in the record establishes anything to the contrary. The

proposed combination of Schultz and Zenhausern thus fails to teach a required element of claim 13, i.e., fluorophores that are mobile within a polymeric matrix. Accordingly, the rejection of claim 13 under 35 U.S.C. § 103 over Schultz in view of Zenhausern has been overcome, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of fluorophores that are mobile within a polymeric matrix.

Claim 14 depends from claim 30 and further specifies that the processor is adapted to store a value corresponding to a property of the detected analyte as a function of time. Neither Schultz nor Zenhausern teaches or suggests a processor that is adapted to store a value corresponding to a property of the detected analyte as a function of time. Nothing in the record establishes anything to the contrary. Schultz and Zenhausern thus fail to teach a required element of the system of claim 14. Accordingly, a *prima facie* case of obviousness of claim 14 has not been made, and the burden has not shifted to Applicant to rebut the same. Thus, the rejection of claim 14 under 35 U.S.C. § 103 over Schultz in view of Zenhausern cannot stand, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a processor that is adapted to store a value corresponding to a property of the detected analyte as a function of time.

Claim 41 depends from claim 30 and further specifies that the third detector is adapted to detect light emitted by skin when the skin is excited by the excitation source. Neither Schultz nor Zenhausern teaches or suggests a third detector adapted to detect light emitted by skin when the skin is excited by the excitation source. Nothing in the record establishes anything to the contrary. The proposed combination of Schultz and Zenhausern thus fails to teach a required element of the system of claim 41. Accordingly, a *prima facie* case of obviousness of claim 41 has not been made and the burden has not shifted to Applicant to rebut the same. Thus, for at least this additional reason, the rejection of claim 41 under 35 U.S.C. § 103 over Schultz in view of Zenhausern cannot stand, and Applicant respectfully requests that it be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action

identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a third detector adapted to detect light emitted by skin when the skin is excited by the excitation source.

Claim 56 is directed to a device that includes a detector-emitter array for detecting an analyte, the detector-emitter array including an excitation source adapted to excite a fluorophore of a sensor that includes fluorophores, and a chip that includes a first detector adapted to detect fluorescence light of a first wavelength emitted by the sensor, a second detector adapted to detect fluorescence light of a second wavelength emitted by the sensor, and a third detector adapted to detect light of a third wavelength, the excitation source being coupled to the chip. Neither Schultz nor Zenhausern teaches or suggests a detector emitter array that includes a chip that includes three detectors and an excitation source coupled to the chip. In addition, neither Schultz nor Zenhausern teaches or suggests a first detector adapted to detect fluorescence light of a first wavelength emitted by a sensor, and a second detector adapted to detect fluorescence light of a second wavelength emitted by the sensor. Nothing in the record establishes anything to the contrary. The proposed combination of Schultz and Zenhausern thus lacks a required element of claim 56. Accordingly, a *prima facie* case of the obviousness of claim 56 has not been made, and the burden has not shifted to Applicant to rebut the same. Therefore, the rejection of claim 56 under 35 U.S.C. § 103 over Schultz in view of Zenhausern cannot stand and must be withdrawn.

The proposed combination of Schultz and Zenhausern is further deficient for at least the following additional reasons. Zenhausern does not teach or suggest detectors that are adapted to detect fluorescence light. To the contrary, the system of Zenhausern does not detect fluorescent light and Zenhausern teaches away from using fluorescence labels (“It is also within the scope of the present invention to use direct detecting an monitoring of biomolecular reactions in real-time without radioactive or fluorescent labeling” Zenhusern, page 3, para [0025]; “Because of the novelty of the present embodiment, some of the severe constraints relative to the use of fluorescent labels.... can be overcome by employing any volatile compound either consumed in a reaction, and/or producing by-products” (*Id.*, para 0073]). Therefore, the skilled artisan would have no reason to modify the system of Schultz to include a chip that includes more than

one detector adapted to detect fluorescent light. For at least this additional reason the rejection of claim 56 under 35 U.S.C. § 103 over Schultz in view of Zenhausern is unwarranted and must be withdrawn. Should this rejection be maintained, Applicant respectfully requests that the next action identify, by reference to page or column and line number, the location in the cited references of a teaching or a suggestion of a chip that includes a detector.

Claims 57-65 are distinguishable under 35 U.S.C. § 103 over Schultz in view of Zenhausern for at least the reasons set forth above in distinguishing claim 56.

Claims 58 and 59 are further distinguishable under 35 U.S.C. § 103 over Schultz in view of Zenhausern for at least the following additional reasons. Claim 58 depends from claim 56 and specifies that the excitation source is adapted to transcutaneously excite a fluorophore of the sensor. Neither Schultz nor Zenhausern teaches or suggests coupling an excitation source that is adapted to transcutaneously excite a fluorophore of a sensor to a chip that includes at least three detectors. Nothing in the record establishes anything to the contrary. The October 18<sup>th</sup> Office action does not provide a reason the skilled artisan would utilize an excitation source that is adapted to transcutaneously excite a fluorophore of a sensor in combination with a chip that includes three detectors. Since this reasoning has not been provided, a *prima facie* case of obviousness has not been made, and the burden has not shifted to Applicant to rebut the same. For at least this additional reason, the rejection of claim 58 under 35 U.S.C. § 103 over Schultz in view of Zenhausern cannot stand, and Applicant respectfully requests that it be withdrawn.

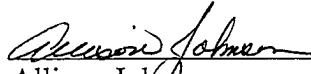
Claim 59 depends from claim 56 and specifies that the detector is adapted to transcutaneously detect light emitted by the sensor. Neither Schultz nor Zenhausern teaches or suggests a chip that includes three detectors in which at least one detector is adapted to transcutaneously detect light emitted by a sensor. Nothing in the record establishes anything to the contrary. Accordingly, a *prima facie* case of obviousness has not been made, and the burden has not shifted to Applicant to rebut the same. For at least this additional reason, the rejection of claim 59 under 35 U.S.C. § 103 over the Schultz in view of Zenhausern is unwarranted, and Applicant respectfully requests that it be withdrawn.

The claims now pending in the application are in condition for allowance, and such action is respectfully requested. The Examiner is invited to telephone the undersigned should a teleconference interview facilitate prosecution of this application.

The Commissioner is hereby authorized to charge any additional fees that may be required and to credit any overpayment to Deposit Account No. 501,171.

Respectfully submitted,

Date: December 18, 2007

  
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